Attorney Docket No.: NUCL-001/01US

**Application No. 10/009,134** 

IN THE CLAIMS

Claims 1-106 (Cancelled).

107. (Currently amended) A multitarget partially double-stranded RNA molecule comprising

two or more different double stranded RNA sequences that are substantially homologous and

complementary to two or more sequences of at least one target mammalian gene or mammalian

pathogen gene, wherein said two or more different double stranded RNA sequences are separated

by cleavage sequences.

108. (Previously presented) The multitarget partially double-stranded RNA molecule of claim

107, wherein said two or more different double stranded RNA sequences are substantially

homologous and complementary to two or more sequences of more than one target gene.

109. (Previously presented) The multitarget partially double-stranded RNA molecule of claim

107, wherein at least 11 to 30 nucleotides of said multitarget partially double-stranded RNA

molecule are involved in each different double-stranded sequence.

110. (Previously presented) The multitarget partially double-stranded RNA molecule of claim

107, wherein each different double stranded RNA sequence comprises at least one segment of 30

contiguous nucleotides with a homology of at least 50% to a similar 30 nucleotide region of the

target sequence, wherein said segment of 30 contiguous nucleotides is also non-homologous to

any naturally occurring and essential polynucleotide sequence.

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111. (Previously presented) The multitarget partially double-stranded RNA molecule of claim

107, wherein said multitarget partially double-stranded RNA molecule is between about 100 and

10,000 polynucleotides in length.

112. (Previously presented) The multitarget partially double-stranded RNA molecule of claim

107, wherein said multitarget partially double-stranded RNA molecule is at least about 200

nucleotides in length.

113. (Previously presented) The multitarget partially double-stranded RNA molecule of claim

107, wherein one or more of said different double stranded RNA sequences comprises a sense

polynucleotide and an antisense polynucleotide separated by a non-base-paired polynucleotide

sequence.

114. (Previously presented) The multitarget partially double-stranded RNA molecule of claim

113, wherein said sense and antisense polynucleotides form a hairpin.

115. (Cancelled)

116. (Currently amended) The multitarget partially double-stranded RNA molecule of claim

107 115, wherein said cleavage sequences are autocatalytic sequences or splice sites.

117. (Previously presented) The multitarget partially double-stranded RNA molecule of claim

107, wherein said at least one target gene is from a single target pathogen.

118. (Previously presented) The multitarget partially double stranded RNA molecule of claim 108, wherein said more than one target genes are from more than one target pathogens.

- 119. (Previously presented) The multitarget partially double-stranded RNA molecule of claim 117, wherein said target pathogen is a virus.
- 120. (Previously presented) The multitarget partially double-stranded RNA molecule of claim 119, wherein said virus is selected from the group consisting of HBV, HIV, HSV, CMV, HPV, HTLV and EBV.
- 121. (Previously presented) The multitarget partially double-stranded RNA molecule of claim 118, wherein said more than one target pathogens are viruses.
- 122. (Previously presented) The multitarget partially double-stranded RNA molecule of claim 121, wherein said more than one viruses are selected from the group consisting of HBV, HIV, HSV, CMV, HPV, HTLV and EBV.
- 123. (Previously presented) The multitarget partially double-stranded RNA molecule of claim 107, wherein said at least one target gene is associated with a disease or disorder in a mammal.
- 124. (Previously presented) The multitarget partially double-stranded RNA molecule of claim123, wherein said at least one target gene is a cancer-associated gene.

125. (Previously presented) The multitarget partially double-stranded RNA molecule of claim

108, wherein said more than one target genes are associated with a disease or disorder in a

mammal.

126. (Previously presented) The multitarget partially double-stranded RNA molecule of claim

125, wherein said more than one target genes are cancer-associated genes.

127. (Previously presented) The multitarget partially double-stranded RNA molecule of claim

107, wherein said two or more sequences of said at least one target gene are selected from the

group consisting of transcribed sequences, non-transcribed sequences, coding sequences, non-

coding sequences, exon-containing sequences, regulatory sequences and promoter sequences.

128. (Previously presented) The multitarget partially double-stranded RNA molecule of claim

107, wherein said multitarget partially double-stranded RNA molecule lacks a poly-adenylation

signal.

129. (Previously presented) A composition comprising the multitarget partially double-

stranded RNA molecule of claim 107.

130. (Previously presented) The composition of claim 129 further comprising an agent which

facilitates polynucleotide uptake by a cell.

131. (Previously presented) A DNA molecule encoding the multitarget partially double-

stranded RNA molecule of claim 107.

132. (Previously presented) An expression vector encoding the multitarget partially double-

stranded RNA molecule of claim 107.

133. (Previously presented) The expression vector of claim 132, wherein said multitarget

partially double-stranded RNA molecule is expressed using a promoter selected from the group

consisting of a mitochondrial promoter, a RNA pol I promoter, a RNA pol II promoter, a RNA

pol III promoter, a viral promoter, a bacterial promoter and a bacteriophage promoter.

134. (Previously presented) The expression vector of claim 133, wherein said multitarget

partially double-stranded RNA molecule is expressed using a RNA pol III promoter.

135. (Previously presented) The expression vector of claim 132, wherein said vector is a

plasmid, phage or recombinant virus.

136. (Previously presented) The expression vector of claim 132, wherein said encoded

multitarget partially double-stranded RNA molecule lacks a poly-adenylation signal.

137. (Cancelled)

138. (Currently amended) The expression vector of claim 132 137 wherein said two or more different double stranded RNA sequences are homologous and complementary to two or more target sequences of more than one target gene.

139. (Currently amended) The expression vector of claim 132 137, wherein the vector encodes two or more different RNA molecules that are multitarget partially double-stranded RNA molecule is at least about 100 nucleotides in length, and wherein each different double-stranded RNA sequence comprises comprising at least 11 to 30 nucleotides involved in the double-stranded sequence.

140. (Currently amended) The expression vector of claim 132 137, wherein each different double-stranded RNA sequence contains at least one segment of 30 contiguous nucleotides with a homology of at least 50% to a similar 30 nucleotide region of the target sequence, wherein said segment of 30 contiguous nucleotides is also non-homologous to any naturally occurring and essential polynucleotide sequence in said cell.

## 141. (Cancelled)

142. (Currently amended) The expression vector of claim 132 141, wherein said multitarget partially double-stranded RNA molecule is between about 100 and 10,000 polynucleotides in length.

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- 143. (Currently amended) The expression vector of claim <u>132</u> 141, wherein said multitarget partially double-stranded RNA molecule is at least about 200 nucleotides in length.
- 144. (Currently amended) The expression vector of claim 132 137, wherein one or more of said different double stranded RNA sequences comprises a sense polynucleotide and an antisense polynucleotide separated by a non-base-paired polynucleotide sequence.
- 145. (Previously presented) The expression vector of claim 144, wherein said sense and antisense polynucleotides form a hairpin.
- 146. (Cancelled)
- 147. (Currently amended) The expression vector of claim 132 146, wherein said cleavage sequences are autocatalytic sequences or splice sites.

Claims 148-156. (Cancelled)

- 157. (Currently amended) The expression vector of claim 132 137, wherein said at least one target gene is from a single target pathogen.
- 158. (Previously presented) The expression vector of claim 138, wherein said more than one target genes are from more than one target pathogens.

- 159. (Previously presented) The expression vector of claim 157, wherein said target pathogen is a virus.
- 160. (Previously presented) The expression vector of claim 159, wherein said virus is selected from the group consisting of HBV, HIV, HSV, CMV, HPV, HTLV and EBV.
- 161. (Previously presented) The expression vector of claim 158, wherein said more than one target pathogens are viruses.
- 162. (Currently amended) The expression vector of claim 161, wherein said more than one viruses <u>are</u> selected from the group consisting of HBV, HIV, HSV, CMV, HPV, HTLV and EBV.
- 163. (Currently amended) The expression vector of claim 132 137, wherein said at least one target gene is associated with a disease or disorder in a mammal.
- 164. (Previously presented) The expression vector of claim 163, wherein said at least one target gene is a cancer-associated gene.
- 165. (Previously presented) The expression vector of claim 138, wherein said more than one target genes are associated with a disease or disorder in a mammal.

166. (Previously presented) The expression vector of claim 165, wherein said more than one target genes are cancer-associated genes.

167. (Currently amended) The expression vector of claim 132 137, wherein said two or more sequences of said at least one target gene are selected from the group consisting of transcribed sequences, non-transcribed sequences, coding sequences, non-coding sequences, exoncontaining sequences, regulatory sequences and promoter sequences.

Claims 168-171. (Cancelled)

- 172. (Currently amended) A composition comprising the expression vector of claim 132 137.
- 173. (Previously presented) The composition of claim 172 further comprising an agent which facilitates polynucleotide uptake by a cell.
- 174. (Currently amended) The expression vector of claim 132 137, wherein the vector encodes two or more different RNA molecules that are multitarget partially double-stranded RNA molecule is less than about 750 nucleotides in length, and wherein each different double-stranded RNA sequence comprises comprising at least 11 to 30 nucleotides involved in the double-stranded sequence.